REMARKS

Claims 38-68 are pending and under examination. Claim 39 has been amended. Support for the amendments can be found throughout the specification and the claims as filed. In particular, support for the amendment can be found, for example, on page 59, lines 5-9. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Rejections Under 35 U.S.C. § 112

The rejection of claims 38, 41 and 42 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. Applicant respectfully maintains that the specification provides sufficient description and guidance to enable claims 38, 41 and 42.

Applicant respectfully maintains, for the reasons of record, that the specification provides sufficient description and guidance for various routes of administration. With regard to targeting lymphoid tissues other than spleen, Applicant respectfully maintains that the Rule 132 Declaration by Dr. Zanetti filed in the response submitted July 29, 2003, corroborates Applicant's position. The Declaration indicates that a large percentage of the cells in various lymphoid tissues are B cells, including 10-15% in peripheral blood, 40-50% in spleen, 20-25% in lymph nodes, and 60-70% in Payer's patches. In the Office Action on page 6, it is acknowledged that spleen cells contain a large number of B cells. However, Applicants respectfully disagree with the assertion that "other tissues, including other lymphoid tissues such as lymph nodes or peripheral blood do not." Clearly as discussed above and in previous responses, various lymphoid tissues contain a large number of B cells. To assert that 10-15%, 20-25% and 60-70% of cells being B cells in peripheral blood, lymph nodes and Payer's patches is not a large number of B cells whereas 40-50% in spleen is a large number of B cells is not tenable.

Based on the presence of a large percentage of B cells in various lymphoid tissues, Applicant respectfully maintains that the expression in B cells exemplified by administration to spleen is enabling for administration to various lymphoid tissues, as attested to by Dr. Zanetti in the previously filed Declaration. Therefore, Applicant respectfully maintains that the specification, in combination with what was well known to those skilled in the art, provides sufficient description and guidance to enable the claimed methods.

Applicant respectfully maintains that the reference by Maloy et al., Proc. Natl. Acad. Sci. USA 98:3299-3203 (2001), which was submitted as Exhibit 2 with the response filed July 29, 2003, corroborates Applicant's position that administration to various lymphoid tissues is enabled by the teachings in the specification. Maloy et al. clearly demonstrates that administration of a nucleic acid vector to lymph nodes resulted in efficient expression of antigen and enhanced immunogenicity. Based on the description in Maloy et al. of superior immunity obtained by intra-lymph node injection, the utilization of a B cell promoter as taught in Applicant's specification and recited in the claims, and the presence of 20-25% B cells in lymph nodes, one skilled in the art would have had a reasonable expectation of successfully stimulating an immune response using the claimed methods.

With respect to the references by Deonarian, Exp. Opin. Ther. Patents 8:53-69 (1998), and Miller et al., FASEB J. 9:190-199 (1995), referred to in the Office Action, Applicant maintains, for the reasons of record, that unpredictability is not an issue with respect to the claimed methods. Applicant respectfully maintains any unpredictability for *in vivo* targeting and expressing genes as described in these general review articles is not applicable to the claimed invention because the claims explicitly recite that the heterologous epitopes are expressed in a B cell and are, therefore, directed to methods where the nucleic acids have been successfully targeted to a B cell and expressed by a B cell.

Applicant maintains that the specification provides sufficient description and guidance to enable the claimed methods. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claim 39 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed. Applicant respectfully submits that claim 39 is clear and definite. Claim 39, as amended, recites "administering B cells of said lymphoid tissue to an individual, wherein said B cells express said one or more heterologous epitopes." Applicants respectfully submit that claim 39 is clear as to which cells are administered and express one or more heterologous epitopes resulting in stimulation of an immune response. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

The rejection of claims 39, 40 and 43-68 under 35 U.S.C. § 103 as allegedly obvious over Soo Hoo, U.S. Patent No. 5,891,432, in view of Banerji et al., Cell 33:729-740 (1983), is respectfully traversed. Applicant respectfully maintains that these claims are unobvious over Soo Hoo, alone or in combination with Banerji et al.

Applicant respectfully maintains, for the reasons of record, that Soo Hoo, alone or in combination with Banerji et al., does not teach or suggest the claimed methods or compositions. Applicant maintains that there would have been no motivation to combine the description in Soo Hoo with that of Banerji et al. to obtain the claimed methods or compositions, absent Applicant's teachings. Furthermore, Applicant respectfully submits that even if one were to combine the description in Soo Hoo with that of Banerji et al., the claimed methods and compositions would not be obtained. In the previous Office Action mailed March 10, 2004, it was asserted that Soo Hoo described using myeloma or plasmacytoma cells and that myeloma and plasmacytoma cells are "transformed B cells." As discussed in the previous response, there is no mention in Soo Hoo of "myeloma."

Furthermore, Applicants respectfully submit that myeloma and plasmacytoma cells are plasma cell tumors, not "transformed B cells." In corroboration, submitted herewith as Exhibit 1 are pages 1165 and 1376 from Stedman's Medical Dictionary, 26th ed., Williams and Wilkins Baltimore (1995), giving the definitions of "myeloma" and "plasmacytoma." The definitions of myeloma and plasmacytoma clearly indicate that these cells are plasma cells, not B cells. As evidence that plasma cells are distinct from B cells, submitted herewith as Exhibit 2 are pages 212 and 216 of Kuby, Immunology, 3rd ed., W.H. Freeman and Company, New York (1997). These pages clearly show that plasma cells are differentiated from B cells but are not themselves B cells. Therefore, even if, *arguendo*, one were to combine the description in Soo Hoo with that of Banerji et al., at best one skilled in the art may have been motivated to use plasma tumor cells, that is, plasmacytoma (Soo Hoo) or myeloma (Banerji et al.). However, the combination of Soo Hoo with Banerji et al. provides no teaching or suggestion of using a B cell, as recited in the claims. Accordingly, Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

Applicants respectfully maintain, for the reasons of record and as discussed above, and as corroborated by the evidence submitted herewith, that Soo Hoo, alone or in combination with Banerji et al., does not teach or suggest Applicant's claimed methods and compositions. Absent such a teaching or suggestion, Applicant maintains that the claimed methods and compositions are unobvious over Soo Hoo, alone or in combination with Banerji et al. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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EXHIBIT 1

STEDMAN'S Medical Dictionary

26th Edition

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my·e·lo·cyte (mī′ĕ-lō-sīt). **1.** A young cell of the granulocytic series, occurring normally in bone marrow, but not in circulating blood (except in certain diseases). When stained with the usual dyes, the cytoplasm is distinctly basophilic and relatively more abundant than in myeloblasts or promyelocytes, even though m.'s are smaller cells; numerous cytoplasmic granules (*i.e.*, neutrophilic, eosinophilic, or basophilic) are present in the more mature forms of m.'s, and the first two types are peroxidase-positive. The nuclear chromatin is coarser than that observed in myeloblasts, but it is relatively faintly stained and lacks a well defined membrane; the nucleus is fairly regular in contour (*i.e.*, not indented), and seems to be "buried" beneath the numerous cytoplasmic granules. **2.** A nerve cell of the gray matter of the brain or spinal cord. SYN medullocell. [myelo- + G. *kytos*, cell]

m. A, the youngest form of m., characterized by only a few (not more than ten) cytoplasmic granules, which are most reliably demonstrated by means of staining with neutral red; the mitochondria are numerous, and resemble those of the myeloblast.

m. B, the intermediate form of m., characterized by approximately 30 to 100 (or more) cytoplasmic granules scattered among the mitochondria; the latter are less numerous than in m.'s of the A stage, and they are frequently displaced toward the periphery of the cell.

m. C, the most mature of the m.'s characterized by numerous cytoplasmic granules that are recognizable as neutrophilic, eosinophilic, and basophilic; with neutral red these are stained, respectively, red, bright yellow, and deep maroon; C m.'s are frequently larger than earlier forms; if the nucleus is indented, the m. is maturing into a metamyelocyte.

my·e·lo·cy·the·mia (mī′ĕ-lō-sī-thē′mē-ă). The presence of myelocytes in the circulating blood, especially in persistently large numbers (as in myelocytic leukemia). [myelocyte + G. *haima*, blood]

my·e·lo·cyt·ic (mī′ĕ-lō-sit′ik). Pertaining to or characterized by myelocytes.

my·e·lo·cy·to·ma (mī′ĕ-lō-sī-tō′mă). A nodular focus or fairly well-circumscribed, relatively dense accumulation of myelocytes, as in certain tissues of persons with myelocytic leukemia. [myelocyte + G. *-oma*, tumor]

my·e·lo·cy·to·ma·to·sis (mī′ĕ-lō-sī′tō-mă-tō′sis). **1.** A form of tumor involving chiefly the myelocytes. SYN leukochloroma. **2.** A rare leukosis of fowl marked by the presence of white tumors composed of myeloid cells, located principally along the sternum and in the liver.

my·e·lo·cy·to·sis (mī′ĕ-lō-sī-tō′sis). The occurrence of abnormally large numbers of myelocytes in the circulating blood, or tissues, or both. [myelocyte + G. *-osis*, condition]

my·e·lo·di·as·ta·sis (mī′ĕ-lō-dī-as′tă-sis). Softening and destruction of the spinal cord. [myelo- + G. *diastasis*, separation]

my·e·lo·dys·pla·sia (mī′ĕ-lō-dis-plā′zē-ă). **1.** An abnormality in development of the spinal cord, especially the lower part of the cord. **2.** Inappropriate term for spina bifida occulta. [myelo- + G. *dys-*, difficult, + *plasis*, a molding]

my·e·lo·fi·bro·sis (mī′ĕ-lō-fī-brō′sis). Fibrosis of the bone marrow, especially generalized, associated with myeloid metaplasia of the spleen and other organs, leukoerythroblastic anemia, and thrombocytopenia, although the bone marrow often contains many megakaryocytes. SYN myelosclerosis, osteomyelofibrotic syndrome.

my·e·lo·gen·e·sis (mī′ĕ-lō-jen′ĕ-sis). **1.** Development of bone marrow. **2.** Development of the central nervous system. **3.** Formation of myelin around an axon.

my·e·lo·ge·net·ic, my·e·lo·gen·ic (mī′ĕ-lō-jĕ-net′ik, -jen′ik). **1.** Relating to myelogenesis. **2.** Produced by or originating in the bone marrow. SYN myelogenous.

my·e·log·e·nous (mī-ĕ-loj′ĕ-nŭs). SYN myelogenetic (2).

my·e·lo·gone, my·e·lo·go·ni·um (mī′ĕ-lō-gōn, mī′ĕ-lo-gō′nē-ŭm). An immature white blood cell of the myeloid series that is characterized by a relatively large, fairly deeply stained, finely reticulated nucleus that contains palely stained nucleoli, and a scant amount of rimlike, nongranular, moderately basophilic cytoplasm. M.'s are difficult to distinguish from lymphoblasts and monoblasts, unless one evaluates them in relation to the more mature forms usually associated with the younger cells. SYN myelogonium. [myelo- + G. *gonē*, seed]

my·e·lo·gram (mī′breve;e-lō-gram). Radiographic contrast study of the spinal subarachnoid space and its contents.

cervical m., contrast medium introduced directly into the cervical subarachnoid space, or moved with the help of gravity from the lumbar region, to outline the cervical cord and nerve roots.

lumbar m., most common study for herniated nucleus pulposus or intervertebral disc protrusion.

my·e·log·ra·phy (mī′ĕ-log′ră-fē). Radiography of the spinal cord and nerve roots after the injection of a contrast medium into the spinal subarachnoid space. [myelo- + G. *graphē*, a drawing]

my·e·lo·ic (mī-ĕ-lō′ik). Pertaining to the tissue and precursor cells from which neutrophils, eosinophils, and basophils are derived.

my·e·loid (mī′ĕ-loyd). **1.** Pertaining to, derived from, or manifesting certain features of the bone marrow. **2.** Sometimes used with reference to the spinal cord. **3.** Pertaining to certain characteristics of myelocytic forms, but not necessarily implying origin in the bone marrow. [myel- + -oid]

my·e·loi·do·sis (mī′ĕ-loy-dō′sis). General hyperplasia of myeloid tissue.

my·e·lo·leu·ke·mia (mī′ĕ-lō-lū-kē′mē-ă). A form of leukemia in which the abnormal cells are derived from myelopoietic tissue.

my·e·lo·li·po·ma (mī′ĕ-lō-li-pō′mă). A misnomer for certain nodular foci that are not neoplasms, but probably represent accumulations of cells derived from localized proliferation of reticuloendothelial tissue in the blood sinuses of the adrenal glands; grossly, the nodules may seem to be adipose tissue, but actually are foci of bone marrow containing erythropoietic or myeloid cells.

my·e·lo·lym·pho·cyte (mī′ĕ-lō-mon′ō-sīt). Rarely used term for an abnormal form of the lymphocytic series in the bone marrow, and presumed to be formed in that tissue.

my·e·lol·y·sis (mī-ĕ-lol′i-sis). Decomposition of myelin.

my·e·lo·ma (mī-ĕ-lō′mă). **1.** A tumor composed of cells derived from hemopoietic tissues of the bone marrow. **2.** A plasma cell tumor. [myelo- + G. *-oma*, tumor]

Bence Jones m., multiple m. in which the malignant plasma cells excrete only light chains of one type (either κ or λ); lytic bone lesions occur in about 60% of the cases, and light chains (Bence Jones protein) occur in the urine; amyloidosis and severe renal failure are more common than in multiple m. SYN L-chain disease, L-chain m.

endothelial m., SYN Ewing's *tumor*.

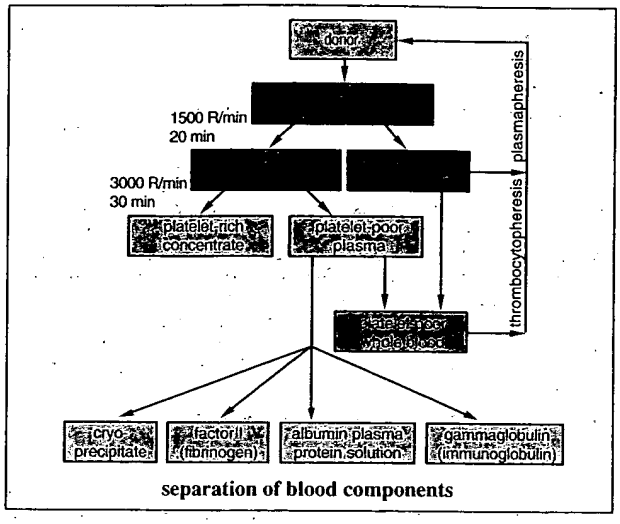
giant cell m., SYN giant cell *tumor* of bone.

L-chain m., SYN Bence Jones m.

multiple m., m. mul'tiplex, an uncommon disease that occurs more frequently in men than in women and is associated with anemia, hemorrhage, recurrent infections, and weakness. Ordinarily, it is regarded as a malignant neoplasm that originates in bone marrow and involves chiefly the skeleton, with clinical features attributable to the sites of involvement and to abnormalities in formation of plasma protein; characterized by numerous diffuse foci or nodular accumulations of abnormal or malignant plasma cells in the marrow of various bones (especially the skull), causing palpable swellings of the bones, and occasionally in extraskeletal sites; radiologically, the bone lesions have a characteristic punched-out appearance. The myeloma cells produce abnormal proteins in the serum and urine; those formed in any one example of multiple m. are different from other m. proteins, as well as from normal serum proteins, the most frequent abnormalities in the metabolism of protein being: 1) the occurrence of Bence Jones proteinuria, 2) a great increase in monoclonal γ-globulin in the plasma, 3) the occasional formation of cryoglobulin, and 4) a form of primary amyloidosis. The Bence Jones protein is not a derivative of abnormal serum protein, but seems to be formed *de novo* from amino acid precursors. SEE ALSO plasma cell m. SYN multiple myelomatosis; myelomatosis multiplex, plasma cell m. (1).

nonsecretory m., multiple m. in which there is no detectable paraproteinemia or paraproteinuria.

plasma cell m., **(1)** SYN multiple m. **(2)** plasmacytoma of bone,



separation of blood components

muscle p., an alkaline fluid in muscle that is spontaneously coagulable, separating into myosin and muscle serum.

normal human p., sterile p. obtained by pooling approximately equal amounts of the liquid portion of citrated whole blood from eight or more adult humans who have been certified as free from any disease which is tranmissible by transfusion, and treating it with ultraviolet irradiation to destroy possible bacterial and viral contaminants.

salted p., the fluid portion of blood drawn from the vessels, which is prevented from coagulating by being drawn into a solution of sodium or magnesium sulfate. SYN salted serum.

plasma-, plasmat-, plasmato-, plasmo-. Formative, organized; plasma. [G. *plasma,* something formed]

plas·ma·blast (plaz′mă-blast). Precursor of the plasma cell. SYN plasmacytoblast. [plasma + G. *blastos,* germ]

plas·ma cell dys·cra·sia. A diverse group of diseases characterized by the proliferation of a single clone of cells producing a monoclonal immunoglobulin or immunoglobulin fragment (a serum M component). The cells usually have plasma cell morphology, but may have lymphocytic or lymphoplasmacytic morphology. This group includes multiple myeloma, Waldenström's macroglobulinemia, the heavy chain disease, benign monoclonal gammopathy, and immunocytic amyloidosis.

plas·ma·crit (plaz′mă-krit). A measure of the percentage of the volume of blood occupied by plasma, in contrast to a hematocrit. [plasma + G. *krinō,* to separate]

plas·ma·cyte (plaz′mă-sīt). SYN plasma *cell.*

plas·ma·cy·to·blast (plas-mă-sī′tō-blast). SYN plasmablast.

plas·ma·cy·to·ma (plaz′mă-sī-tō′mă). A discrete, presumably solitary mass of neoplastic plasma cells in bone or in one of various extramedullary sites; in man, such lesions are probably the initial phase of developing plasma cell myeloma. [plasmacyte + G. *-oma,* tumor]

plas·ma·cy·to·sis (plaz′mă-sī-tō′sis). **1.** Presence of plasma cells in the circulating blood. **2.** Presence of unusually large proportions of plasma cells in the tissues or exudates. [plasmacyte + G. *-osis,* condition]

plas·ma ex·pand·er (plaz′mă eks-pan′der). SYN plasma *substitute.*

plas·ma·gene (plaz′mă-jēn). A determinant of an inherited character located in the cytoplasm. SYN cytogene. [plasma + gene]

plas·ma·ki·nins (plaz′mă-kīn′inz). A group of highly active oligopeptides found in sera that act upon smooth muscle of blood vessels, uterus, bronchi, etc.; *e.g.,* bradykinin, kallidin.

plas·ma·lem·ma (plaz-mă-lem′ă). SYN cell *membrane.* [plasma + G. *lemma,* husk]

plas·mal·o·gens (plaz-mal′ō-jenz). Generic term for glycerophospholipids in which the glycerol moiety bears a 1-alkenyl ether group (on rarer occasions, a 1-alkyl ether group); e.g., alk-1-enylglycerophospholipid; p. synthesis is reduced in disorders of the peroxisome. SYN phosphoglyceracetals.

plas·mals (plaz′mălz). Long-chain aldehydes occurring in plasmalogens; *e.g.,* stearaldehyde, palmitaldehyde.

plas·ma·phe·re·sis (plaz′mă-fĕ-rē′sis). Removal of whole blood from the body, separation of its cellular elements by centrifugation, and reinfusion of them suspended in saline or some other plasma substitute, thus depleting the body's own plasma without depleting its cells. [plasma + G. *aphairesis,* a withdrawal]

plas·ma·phe·ret·ic (plaz′mă-fĕ-ret′ik). Relating to plasmapheresis.

blood plasma

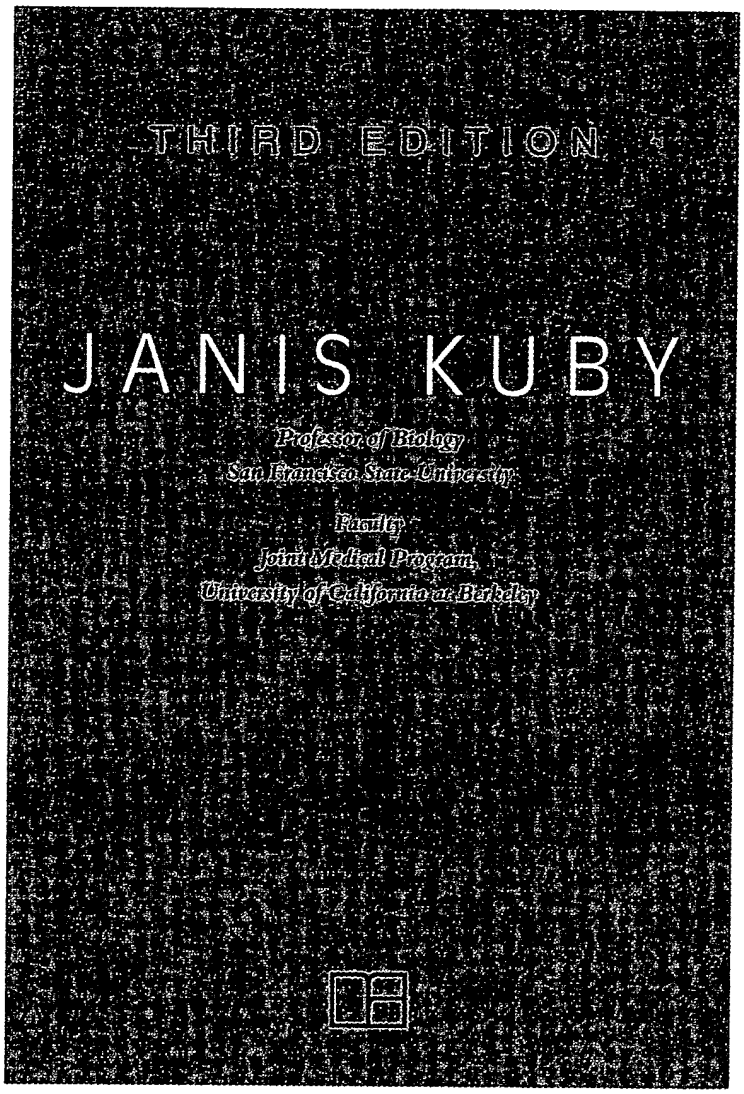
selected components of plasma or serum: normal parameters

ammonia *N* (whole blood)	53-143	µmol/l
bicarbonate	21-25	mmol/l
bilirubin (total)	5.1-18.8	µmol/l
bilirubin (direct)	up to 6.8	µmol/l
lead (whole blood)	up to 2.0	µmol/l
blood sugar: see glucose		
calcium	2.2-2.7	mmol/l
chloride	94-111	mmol/l
cholesterin	3.36-6.72*	mmol/l
creatine	♂ 23-61	µmol/l
	♀ 23-92	
creatinine	♂ 62-106	µmol/l
	♀ 44-88	
iron	♂ 16.1-25.1	µmol/l
	♀ 14.3-21.5	
iron binding capacity		
–total	♂ 53.7-71.6	µmol/l
	♀ 44.8-62.7	
–free	♂ 35.8-53.7	µmol/l
	♀ 26.9-44.8	
protein, total	67-87	g/l
fat, total	3.6-8.2*	g/l
fatty acids, free	200-900	µmol/l
fructose	up to 0.55	mmol/l
galactose	up to 0.24	mmol/l
glucose	3.33-5.55*	mmol/l
glycerine, total	0.27-2.88	mmol/l
glycerine, free	up to 0.25	mmol/l
uric acid	♂ 155-404	µmol/l
(enzymatic)	♀ 119-375	
urea	3.33-6.66	mmol/l
potassium	4.1-5.6	mmol/l
copper	♂ 11.0-22.0	µmol/l
	♀ 13.4-24.4	g/l
β-lipoproteide	3.6-6.4*	µmol/l
lithium	0.4-6.3	mmol/l
magnesium	0.66-0.90	mmol/l
lactate	1.00-1.78	mmol/l
sodium	137-148	mmol/l
phosphatide	1.74-3.94	mmol/l
inorganic phosphorus	0.81-1.55	mmol/l
thyroxine	66-187	mmol/l
triglyceride	0.97-2.70*	

*age-dependent

EXHIBIT 2

IMMUNOLOGY



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ABOUT THE COVER AND FRONTISPIECE

Interactions of cell adhesion molecules, with different ones involved at different times, are responsible for recruiting leukocytes to inflammatory sites and for their migration through the vascular endothelium. Slowed by vasodilation, leukocytes drift against vessel walls, where selectins are responsible for a loose adherence known as "rolling." This initial step in leukocyte migration is shown in a false-color scanning electron micrograph. (See Chapter 15 for more information.)

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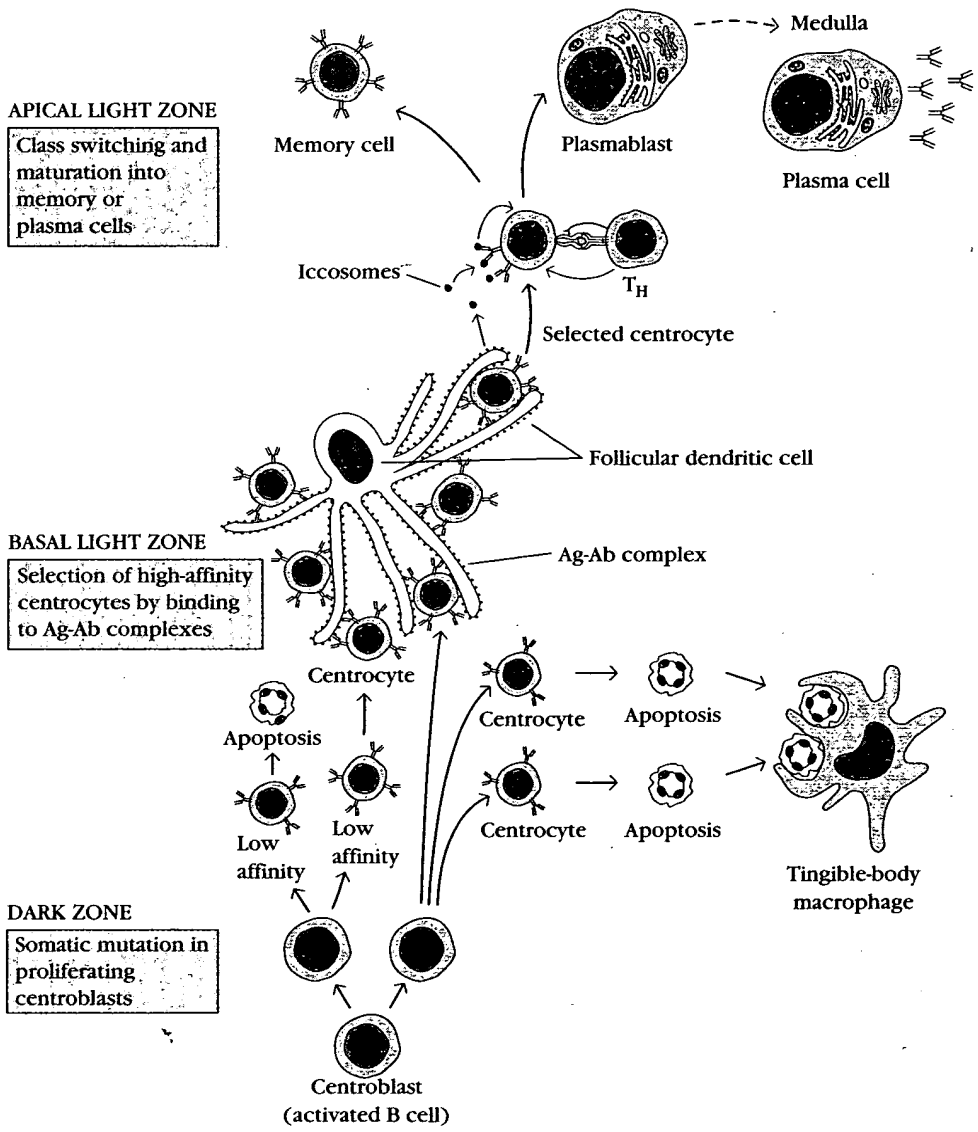

FIGURE 8-16

Overview of cellular events within secondary follicles of peripheral lymph nodes. Follicular dendritic cells bind antigen-antibody complexes along their long processes. Small B cells (centrocytes) bearing high-affinity membrane immunoglobulin (mIg antibodies shown in blue) are thought to interact with antigen presented on the follicular dendritic cells; unselected centrocytes bearing low-affinity mIg die by apoptosis and the debris is phagocytosed by tingible-body macrophages. Selected centrocytes, which may undergo class switching, then mature into memory B cells or plasmablasts; the latter migrate to the medulla where they develop into plasma cells.

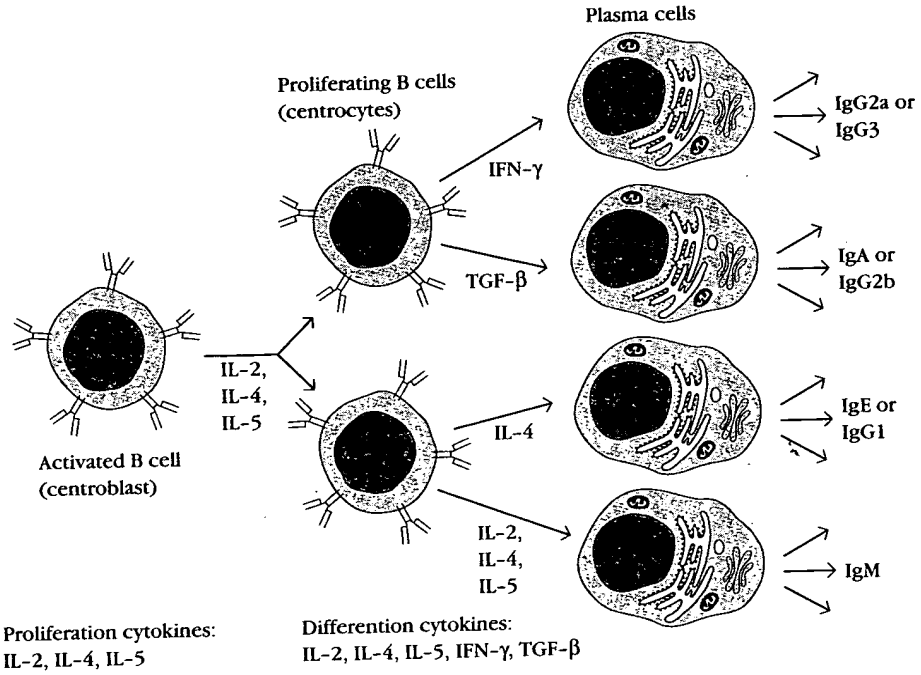

FIGURE 8-19

Numerous cytokines participate in B-cell proliferation and class switching during differentiation into plasma cells. Binding of the proliferation cytokines, which are released by activated T_H cells, provide the progression signal needed for proliferation of activated B cells. The indicated cytokine effects have been demonstrated; however, similar or identical effects may be mediated by other cytokines. Class switching in the response to thymus-dependent antigens also requires the CD40/CD40L interaction, which is not indicated here.

on the action of specific cytokines (Figure 8-19). Cytokines induce class switching by making the switch sites that lie 5′ to each C_H gene accessible, so that switch recombinase enzymes can bind to the site (see Figure 7-12). Exposure of activated B cells to IL-4, for example, results in DNA transcription upstream from the switch regions for $C_\gamma 1$ or C_ε, indicating that the chromatin at these switch sites is now accessible.

In the humoral response to type 1 thymus-independent (TI-1) antigens, class switching does not occur. In the response to TI-2 antigens, class switching to other isotypes can occur, although IgM is the predominant isotype produced. Several cytokines, notably IL-4, IFN-γ, and TGF-β have been shown to be required for class switching in the response to TI-2 antigens. These cytokines are produced by T_H cells, but they can also be produced by other cells enabling class switching during the response to TI-2 antigens even in the absence of T_H cells. Natural killer cells, for example, secrete both IL-4 and IFN-γ, and macrophages and B cells secrete TGF-β.

Class switching is also influenced by the microenvironment of the plasma cell. Plasma cells leaving the follicles of Peyer's patches or mesenteric lymph nodes are almost all committed to IgA production. In contrast, plasma cells originating in the tonsils, spleen, or peripheral lymph nodes are mainly committed to IgG production.

Generation of Plasma Cells and Memory B Cells

Following selection of centrocytes bearing high-affinity mIg for antigen displayed on follicular dendritic cells, the centrocytes differentiate into plasma cells and memory B cells in the apical light zone (see Figure 8-16). It appears that different membrane signals may determine whether a plasma cell or a memory cell is formed, as depicted in Figure 8-20.

Formation of plasma cells is thought to be induced by IL-1 and CD23, which are produced by follicular dendritic cells. CD23 is expressed in a membrane form and is also released in a soluble form, which acts in a paracrine fashion on nearby centrocytes. As noted earlier, CD23 is a ligand for the CR2 component of the co-receptor complex on the B cell. The interaction of either membrane or soluble CD23 with CR2 on the B cell, together with an IL-1 signal, induces the centrocyte to differentiate into a plasma cell.

Plasma cells generally lack detectable membrane-bound immunoglobulin and instead synthesize high levels of secreted antibody. Differentiation of mature B cells into plasma cells must involve a change in RNA processing so that the secreted form of the heavy chain rather than the membrane form is synthesized (see